

P Quinodimethanes Very Important Paper

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Zirconacyclopentadiene-Annulated Polycyclic Aromatic Hydrocarbons

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Abstract: Syntheses of large polycyclic aromatic hydrocarbons (PAHs) and graphene nanostructures demand methods that are capable of selectively and efficiently fusing large numbers of aromatic rings, yet such methods remain scarce. Herein, we report a new approach that is based on the quantitative intramolecular reductive cyclization of an oligo(diyne) with a low-valent zirconocene reagent, which gives a PAH with one or more annulated zirconacyclopentadienes (ZrPAHs). The efficiency of this process is demonstrated by a high-yielding fivefold intramolecular coupling to form a helical ZrPAH with 16 fused rings (from a precursor with no fused rings). Several other PAH topologies are also reported. Protodemetalation of the ZrPAHs allowed full characterization (including by X-ray crystallography) of PAHs containing one or more appended dienes with the ortho-quinodimethane (o-QDM) structure, which are usually too reactive for isolation and are potentially valuable for the fusion of additional rings by Diels-Alder reactions.

he isolation of graphene and the elucidation of its extraordinary properties (e.g., ballistic charge transport, mechanical strength, transparency, and flexibility) have motivated a surge of research on large polycyclic aromatic hydrocarbons (PAHs), which can be considered to be basic building blocks of graphene and other carbon-rich nanostructures.^[1,2] Thus significant attention has focused on PAHs as molecular models for, or synthetic precursors of, this promising class of materials.^[3–5] Large PAHs are also attractive as components of electronic and optoelectronic devices.^[6–9] Their suitability for this purpose is due not only to their unique electronic and photophysical properties,^[10] which result from their extended conjugation and rigidity, but also to their tendency to assemble into highly ordered structures in the solid state.^[11]

A central challenge for investigations of large PAHs is the difficulty associated with the synthesis of pure, well-defined structures, which requires the selective fusion of many aromatic rings.^[12] Near-quantitative yields are necessary for each ring-fusion event to avoid difficult separations and/or defects. To date, the most successful approach is based on the cyclodehydrogenation reaction popularized by Müllen and co-workers, but there are significant limitations with respect

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to regioselectivity and functional-group tolerance.^[4,13] Given the ability of transition metals to facilitate selective and highyielding transformations, they provide a promising platform for the challenging ring-fusion step. Although the development of organometallic methods (e.g., ring-closing alkene metathesis^[14] and [2+2+2] cycloadditions^[15,16]) has received much attention,^[17] few are efficient enough for application to very large PAHs.

We have previously reported the synthesis of π -conjugated oligomers,^[18] polymers,^[19] and macrocycles^[20] through the reductive coupling of alkynes with a low-valent zirconocene reagent. Given its ability to form new rings in high yield, this reaction should be well-suited for PAH syntheses. Takahashi and co-workers demonstrated its application to the iterative elongation of an acene (Scheme 1 a); however,





b) Wang: Annulation of naphthalene diimide with zirconacyclopentadiene



c) Müller: Rhodacyclopentadiene-annulated PAHs



Scheme 1. Previously reported approaches for the synthesis of PAHs with zirconacyclopentadiene and rhodacyclopentadiene synthons. Cp = cyclopentadienyl.

the strategy is lengthy and requires a post-ring-fusion oxidation step.^[21] Wang and co-workers employed zirconacyclopentadienes in the annulation of naphthalene diimides, but alkyne coupling was not involved in the ring-fusion event (Scheme 1b).^[22] A related and potentially far-reaching approach was indicated more than 40 years ago by Müller,^[23] who used diynes with π -conjugated tethers to access several fully unsaturated fused-ring systems via a rhodacyclopentadiene synthon (e.g., **A**; Scheme 1c). Two promising features of this chemistry are that 1) a PAH is

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directly obtained from the precursor (e.g., no subsequent oxidation is required) and 2) functionality can be divergently introduced using metal-transfer reactions. Surprisingly, this approach has been employed for only a limited number of PAHs, which were synthesized via organometallic intermediates containing a single annulated metallacyclopenta-diene.^[24,25]

Herein, we report a generalization of Müller's approach, enabled by the high efficiency of zirconocene coupling. Specifically, the quantitative intramolecular reductive cyclization of an oligo(diyne) (\mathbf{B} ; Scheme 2a) with a low-valent



Scheme 2. Synthetic strategy explored in this work and accessible PAHs.

zirconocene reagent gives a zirconacyclopentadiene-annulated PAH ("ZrPAH", 1). Eleven ZrPAHs (1a-1k; Scheme 2b), representing seven different PAH topologies, are presented, including one with 16 fused rings and five appended zirconacyclopentadiene rings (1k). Importantly, these ZrPAHs result from precursors that have no fused rings and could thus be easily assembled using established C-C bond-forming reactions. Furthermore, high-yielding and stereoselective protodemetalation of 1a-1k was exploited as a novel entry to several PAHs with exocyclic diene functional groups (2a-2k). Such compounds might be expected to exhibit high reactivity, as is typically the case for dienes with the *ortho*-quinodimethane (*o*-QDM; Figure 1) structure.^[26] However, they are remarkably stable when incorporated into a PAH framework (with certain R substituents), which allowed the isolation and full characterization of eight rare



Figure 1. Resonance structures of o-QDM and a benzannulated o-QDM.

examples (**2a–2c** and **2g–2k**). These isolable *o*-QDMs are not only interesting from a fundamental perspective but they can also be selectively hydrogenated using a simple procedure to produce highly alkylated PAHs.

Investigations began with the model system shown in Scheme 3, which involves the reductive coupling of a diyne (3–7) to form a phenanthrene annulated with a single zirconacyclopentadiene (ZrPAHs **1a–1e**). There were two initial goals, namely 1) to establish efficient conditions for the zirconocene coupling, which needs to be very high-yielding to be applied in multifold coupling reactions, and 2) to deter-



Scheme 3. Investigations on a model system. * Yields of isolated products. ZrPAHs **1a** and **1c-1e** were formed quantitatively according to ¹H NMR spectroscopy (the formation of **1b** was not monitored).

mine the suitability of these ZrPAHs as precursors to o-QDMs, which might then be employed in Diels–Alder reactions for fusion of additional rings. Towards this end, ZrPAH **1a** was isolated in 92 % yield after treatment of diyne **3** with Cp₂Zr(pyr)(Me₃SiC \equiv CSiMe₃) (1.1 equiv),^[27] a convenient, well-defined source of "Cp₂Zr".^[28] Monitoring by ¹H NMR spectroscopy revealed that this reaction is rapid (complete in < 5 min) and quantitative.

Treatment of **1a** with excess HCl (5 equiv) produced a surprisingly persistent species consistent with **2a** (as judged by a characteristic quartet at $\delta = 5.7$ ppm and the corresponding doublet at $\delta = 1.8$ ppm for the vinyl and methyl protons, respectively) in nearly quantitative yield. Observation of this species despite the presence of excess strong acid is remarkable; however, 70% of **2a** decomposed to an unidentified product within 6 h. Replacement of HCl with benzoic acid

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The stability of **2a** in solution motivated its isolation as examples of isolable o-QDMs are very rare and invariably involve substitution patterns that preclude their use as synthetic intermediates.^[29,30] Treatment of 1a with excess benzoic acid afforded pure 2a as a colorless crystalline solid after a simple filtration of the reaction mixture diluted with hexanes through a plug of silica gel. The stability of 2a permitted its full characterization, including by X-ray crystallography, which revealed its "twisted" nature in the solid state (Figure 2a). This twist can be quantified by two angles: 1) the torsion angle of the exocyclic diene unit (51.3°) and 2) the twist angle of the biphenyl backbone (19.8°). Compound 2a can be handled for a few hours in air (in solution or as a solid) without detectable decomposition, but prolonged exposure to air at ambient temperature (ca. 21 °C) leads to slow decomposition, probably by O2-catalyzed oligomerization. The solid can be stored indefinitely under a nitrogen atmosphere at ambient temperature. In the absence of O_2 , ring closure to cyclobutarene 8 (Scheme 3) is the major decomposition pathway, but heating to 100 °C for 24 h was required for complete conversion. In contrast, the unsubstituted analogue 9 could not be isolated and has been reported to rapidly decompose by [4+2] dimerization.^[31]

The analogous *n*-propyl-substituted *o*-QDM **2b** was prepared in 95% yield by insitu generation of 1b using Negishi's Cp₂ZrCl₂/"BuLi reagent,^[32] followed by treatment with aqueous HCl. This high yield was possible despite the use of excess strong acid, but short reaction times (< 10 min) were required. Successful isolation of SiMe₃-substituted o-QDM 2c required stoichiometric HCl as this compound rapidly reacted with excess HCl to form an unidentified product. Employment of benzoic acid gave a mixture containing only a small amount of 2c (ca. 10%).

An attempt to isolate diaryl-substituted o-QDM 2d instead led to cyclobutarene 10 as the sole product upon protodemetalation of 1d with HCl, likely through electrocvclic ring closure of 2d. Treatment with benzoic acid gave a complex mixture. An intermediate case was mono-aryl-

substituted o-QDM 2e, which cyclized to 11 with a half-life of about two days at 19°C upon protodemetalation of 1e with HCl. The intermediate 2e was identified by ¹H NMR spectroscopy in 93% yield. It is well known that aryl groups lower the barrier for this reversible ring-closing reaction.^[33]

Thiophene-annulated o-QDM 2f (Scheme 4) was predicted to be more reactive than its benzannulated analogue 2a for two reasons, namely 1) the diminished steric interaction between the methyl groups and annulated rings and 2) the lower aromaticity of the annulated thiophene rings. Indeed, generation of ZrPAH 1f from divne 12 followed by its in situ protodemeta-

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2f

13

no

dienophile

lation led to rapid (< 5 min) 1,4-addition of HCl to yield 13 as the major product. The intermediacy of **2 f** was supported by the isolation of Diels-Alder adduct 14 in 76% yield (in one pot, from 12) upon protodemetalation in the presence of N-ethylmaleimide at 21 °C. In contrast, the analogous Diels-Alder reaction with 2a (Scheme 4) required elevated temperature to proceed at a reasonable rate (70 °C for 15 h). The low reactivity of 2a in the presence of a good dienophile is surprising, but the adduct 15 forms quantitatively and was isolated in high yield (90%). Compound 13 is not a precursor to 14 as addition of *N*-ethylmaleimide after generation of 2 f resulted only in isolation of 13. Importantly, the efficient onepot reaction to form 14 from 12 suggests that this method

1f

Et

14, 76% (one pot,

Scheme 4. Diels-Alder reactivity of the thiophene-annulated o-QDM 2f and comparison with its

0

HCl(aq), MeOH

21 °C

1.2 equiv Et

excess

Et

-0

03





Figure 2. Crystal structures of 2a, 2g, 2h, and 2i. Thermal ellipsoids

set at 50% probability.

1) 2 ⁿBuLi

Et

15.90%

2 equiv

Et

70 °C, 15 h

0-N ~0

benzannulated analogue **2a**.

2a

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should also be of value for more traditional, reactive *o*-QDM chemistry.

The extension of this approach to larger polyaromatic systems by multifold coupling reactions began with precursor bis(diyne)s **16–18** (Scheme 5). These compounds were easily accessible by Suzuki couplings (see the Supporting Informa-



Scheme 5. Twofold couplings for the synthesis of compounds 2g-2i.

tion). Methyl substituents were chosen to simplify structural analysis and promote the crystallinity of the target bis(o-QDM)s. Upon treatment of 16–18 with $Cp_2Zr(pyr)(Me_3SiC \equiv$ CSiMe₃) (2.2 equiv) followed by excess benzoic acid, bis(o-QDM)s 2g-2i were isolated in high yields. The intermediate ZrPAHs 1g-1i were isolated as crude solids, resuspended in benzene or toluene, and then treated with benzoic acid, but isolation of the ZrPAH is optional. While Cp₂Zr-(pyr)(Me₃SiC=CSiMe₃) is an extremely convenient reagent (especially on a small scale), the Negishi protocol (see above) is often preferred. Thus, to demonstrate both the scalability and applicability of this protocol, it was employed to isolate 1.5 g of 2g (89% yield). The structures of 2g-2i were elucidated by X-ray crystallography (Figure 2b-d). Each diene unit was found to possess a similar amount of distortion as 2a, as determined by their diene torsion and biphenyl twist angles. They also have qualitatively similar stabilities. To the best of our knowledge, these are the first examples of isolable compounds with more than one o-QDM subunit.

The isolable *o*-QDMs are structurally fascinating, but their promise for post-coupling functionalization is perhaps of

greater interest. Diels–Alder reactions are the obvious choice; however, initial difficulties with the aromatization of **15** prompted the establishment of an alternative route to valuable functionality. A 1,4-addition of H_2 across the diene is potentially the simplest transformation and would give unique PAHs decorated with alkyl groups. Such functionality, which is currently difficult to install, improves solubility and often promotes liquid crystallinity, with minimal perturbation of electronic properties. A selective 1,4-addition was observed upon exposure of **2a**, **2b**, and **2g–2i** to 1 atm of H_2 over Pd/C to furnish the alkylated PAHs **19–23** in good to very high yields (Scheme 6). A wide range of alkylated PAHs are now within reach using this approach.



Scheme 6. Hydrogenation of 2a, 2b, and 2g–2j.

As a test for the applicability of the method to more demanding multifold couplings, PAHs containing three and five *o*-QDM units were targeted (**2j** and **2k**; Scheme 7). Remarkably, treatment of tris(diyne) **24** and pentakis(diyne) **25** with Cp₂Zr(pyr)(Me₃SiC=CSiMe₃ (3.3 and 5.5 equiv), followed by excess benzoic acid, furnished **2j** and **2k** in excellent yields (89 and 83%) after isolation. Structural evidence was provided by the characteristic ¹H NMR spectra of these isolable *o*-QDMs (see above). The synthesis of the helical PAH **2k** not only demonstrates the high efficiency of the method, but this compound is also the first member of a new class of helicenes with alternating angular and linear fusion. Hydrogenation of **2j** furnished the angular PAH **26** (Scheme 6) in 66% yield.

In conclusion, the method presented herein is a highly efficient means to fuse multiple rings into PAHs that contain valuable zirconacyclopentadiene functional groups (ZrPAH). Protodemetalation of these ZrPAHs gives a new entry to PAHs containing embedded *o*-QDMs. The high yields of these reactions suggest their suitability for the synthesis of even larger PAHs and graphene nanostructures. The discovery of a general class of isolable *o*-QDMs, which are usually generated as fleeting intermediates, opens new possibilities, including reactions with other reactive intermediates (e.g., arynes) or precise control of stoichiometry (e.g., for a Diels-

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Scheme 7. Threefold and fivefold couplings.

Alder polymerization). Finally, and perhaps most importantly, these ZrPAHs are poised for use in any of the known zirconocene transfer reactions and should provide direct access to large heteroatom-functionalized PAHs and carbonrich nanostructures.^[34]

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Conflict of interest

The authors declare no conflict of interest.

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- A. K. Geim, Science 2009, 324, 1530– 1534.
- [2] M. M. Haley, R. R. Tykwinski, Carbon-Rich Compounds: From Molecules to Materials, Wiley-VCH, Weinheim, 2006.
- [3] A. Konishi, Y. Hirao, K. Matsumoto, H. Kurata, R. Kishi, Y. Shigeta, M. Nakano, K. Tokunaga, K. Kamada, T. Kubo, J. Am. Chem. Soc. 2013, 135, 1430–1437.
- [4] A. Narita, X.-Y. Wang, X. Feng, K. Müllen, *Chem. Soc. Rev.* 2015, 44, 6616-6643.
- [5] Y. Segawa, H. Ito, K. Itami, *Nat. Rev. Mater.* 2016, 1, 15002.
- [6] J. Wu, W. Pisula, K. Müllen, Chem. Rev. 2007, 107, 718–747.
- [7] W. Jiang, Y. Li, Z. Wang, Chem. Soc. Rev. 2013, 42, 6113–6127.
- [8] Z. Sun, Q. Ye, C. Chi, J. Wu, Chem. Soc. Rev. 2012, 41, 7857–7889.
- [9] M. Ball, Y. Zhong, Y. Wu, C. Schenck, F. Ng, M. Steigerwald, S. Xiao, C. Nuckolls, *Acc. Chem. Res.* 2015, 48, 267–276.
- [10] R. Rieger, K. Müllen, J. Phys. Org. Chem. 2010, 23, 315-325.

[11] S. Sergeyev, W. Pisula, Y. H. Geerts,

- Chem. Soc. Rev. 2007, 36, 1902–1929.
- [12] M. B. Goldfinger, K. B. Crawford, T. M. Swager, J. Am. Chem. Soc. 1997, 119, 4578–4593.
- [13] B. T. King, J. Kroulík, C. R. Robertson, P. Rempala, C. L. Hilton, J. D. Korinek, L. M. Gortari, J. Org. Chem. 2007, 72, 2279–2288.
- [14] M. C. Bonifacio, C. R. Robertson, J.-Y. Jung, B. T. King, J. Org. Chem. 2005, 70, 8522–8526.
- [15] F. Teplý, I. G. Stará, I. Starý, A. Kollárovič, D. Šaman, L. Rulíšek, P. Fiedler, J. Am. Chem. Soc. 2002, 124, 9175–9180.
- [16] S. Han, A. D. Bond, R. L. Disch, D. Holmes, J. M. Schulman, S. J. Teat, K. P. C. Vollhardt, G. D. Whitener, *Angew. Chem. Int. Ed.* 2002, 41, 3223–3227; *Angew. Chem.* 2002, 114, 3357–3361.
- [17] T. Jin, J. Zhao, N. Asao, Y. Yamamoto, Chem. Eur. J. 2014, 20, 3554–3576.
- [18] M. C. Suh, B. Jiang, T. D. Tilley, Angew. Chem. 2000, 112, 2992– 2995.
- [19] B. L. Lucht, S. S. H. Mao, T. D. Tilley, J. Am. Chem. Soc. 1998, 120, 4354–4365.
- [20] V. H. Gessner, J. F. Tannaci, A. D. Miller, T. D. Tilley, Acc. Chem. Res. 2011, 44, 435–446.
- [21] T. Takahashi, S. Li, W. Huang, F. Kong, K. Nakajima, B. Shen, T. Ohe, K. Kanno, J. Org. Chem. 2006, 71, 7967–7977.
- [22] W. Yue, J. Gao, Y. Li, W. Jiang, S. Di Motta, F. Negri, Z. Wang, J. Am. Chem. Soc. 2011, 133, 18054–18057.
- [23] E. Müller, Synthesis 1974, 761-774.
- [24] a) For an example based on a zirconacyclopentadiene intermediate, see: P.-A. Bouit, A. Escande, R. Szűcs, D. Szieberth, C. Lescop, L. Nyulászi, M. Hissler, R. Réau, *J. Am. Chem. Soc.* 2012, *134*, 6524–6527; b) for an example based on a rhodacyclopentadiene intermediate, see: X. Guo, S. Wang, V. Enkelmann, M. Baumgarten, K. Müllen, *Org. Lett.* 2011, *13*, 6062–6065.
- [25] There are several reports based on the catalytic [2+2+2] reaction that are conceptually analogous to this approach; for examples, see: a) Y.-T. Wu, T. Hayama, K. K. Baldridge, A. Linden, J. S. Siegel, *J. Am. Chem. Soc.* 2006, *128*, 6870–6884; b) A. McIver, D. D. Young, A. Deiters, *Chem. Commun.* 2008, 4750–4752.

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- [26] J. L. Segura, N. Martín, Chem. Rev. 1999, 99, 3199-3246.
- [27] U. Rosenthal, A. Ohff, W. Baumann, A. Tillack, H. Görls, V. V. Burlakov, V. B. Shur, Z. Anorg. Allg. Chem. 1995, 621, 77–83.
- [28] J. R. Nitschke, S. Zürcher, T. D. Tilley, J. Am. Chem. Soc. 2000, 122, 10345–10352.
- [29] a) F. Toda, K. Tanaka, M. Matsui, *Tetrahedron Lett.* 1982, 23, 217–220; b) T. Suzuki, Y. Sakano, T. Iwai, S. Iwashita, Y. Miura, R. Katoono, H. Kawai, K. Fujiwara, Y. Tsuji, T. Fukushima, *Chem. Eur. J.* 2013, 19, 117–123.
- [30] The annulated aromatic rings are one reason for the higher stability of **2a** compared to non-annulated *o*-QDMs. This can be explained by invoking Clar's rules, which predict that the diradical resonance structure (Figure 1) is much less important

in describing the electronic structure of **2a** than for analogous non-benzannulated *o*-QDMs.

- [31] J. P. Anhalt, E. W. Friend, E. H. White, J. Org. Chem. 1972, 37, 1015–1019.
- [32] E. Negishi, F. E. Cederbaum, T. Takahashi, *Tetrahedron Lett.* 1986, 27, 2829–2832.
- [33] A. K. Sadana, R. K. Saini, W. E. Billups, Chem. Rev. 2003, 103, 1539–1602.
- [34] X. Yan, C. Xi, Acc. Chem. Res. 2015, 48, 935-946.

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Zirconacyclopentadiene-Annulated Polycyclic Aromatic Hydrocarbons



Zirconocene zipper: An efficient fivefold reductive cyclization demonstrates the promise of a new strategy for the construction of graphene nanostructures. Protodemetalation of the resulting zirco-



nacyclopentadiene-annulated polycyclic aromatic hydrocarbons provides a conceptually unique means for the generation of valuable *ortho*-quinodimethane structures.

